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EXAMINER	
STEADMAN, DAVID J	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,752	IKEDA, KEIKO	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *5 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/8/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendix A, sequence alignment*.

DETAILED ACTION

Status of the Application

[1] Claims 1-9 are pending in the application.

Lack of Unity

[2] Applicant's election with traverse of Group I, claims 1-4 and 6-8, in the reply filed on 10/9/07 is acknowledged. The traversal is on the ground(s) that "Groups I to III satisfy the combination of categories provided at 37 CFR 1.475(b)". This is not found persuasive, because, as noted in the prior Office action and undisputed by applicant,

> "According to PCT Rule 13.2 unity of invention exists only when the shared same or corresponding special technical feature is a contribution over the prior art. The inventions listed as Groups I-III do not relate to a single general inventive concept because they lack the same or corresponding special technical feature. The technical feature of Group I is a protein complex and the technical feature of Group II is a method for producing a protein complex, which are shown by Ikeda et al. (*J. Virol.* 75:988-995, 2001; cited in the IDS filed on 7/8/05) to lack novelty or inventive step because the reference teaches a protein complex encompassed by claim 1 (see particularly the BmCPV polyhedrin-encapsulated GFP protein fused to BmVP3 at, *e.g.,* p. 994, column 1) and a method of making said protein complex, and thus the shared same or coresponding special technical feature of Groups I-II is not a contribution over the prior art."

Specifically regarding claim 9, it was noted in the prior Office action and undisputed by applicant:

> It is noted that the "immobilized enzyme" and the "target protein" in claim 9 are unrelated, *i.e.,* there is no recited association between the "immobilized enzyme" and the "target protein." For purposes of restriction, claim 9 has been interpreted as being drawn only to "an immobilized enzyme packed in a container" and the "wherein" clause does not further limit the "immobilized enzyme" or require its association with the "target protein" in any way.

In this case, the invention of Group I and the invention of Group III do not share the same or corresponding special technical feature. In this case, each of Groups I and III has a different special technical feature as the special technical feature of Group I is a protein complex and the special technical feature of Group III is an immobilized enzyme. Moreover, each of the inventions of Groups I and III was known in the art at the time of the invention and thus do not make a contribution over the prior art. According to 37 CFR 1.475, "If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims".

Accordingly, the requirement is still deemed proper and is therefore made FINAL.

[3] Claims 5 and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/9/07.

Priority

[4] Applicant's claim to foreign priority under 35 USC § 119(a)-(d) to Japanese application JP 2003-005099, filed on 1/10/03, is acknowledged. A certified copy of the

foreign priority document has been filed in the instant application on 7/8/05. The priority claim is set forth in the Declaration filed under 37 CFR 1.63 on 2/7/06.

Information Disclosure Statement

[5] With the exception of references AG, AI, and AJ, all references cited in the IDS filed on 7/8/05 have been considered by the examiner. A copy of Form PTO/SB/08 is attached to the instant Office action. References AG, AI, and AJ of the IDS have not been considered as a copy of each reference has not been provided as required by 37 CFR 1.98(d).

Specification/Informalities

[6] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: -- Cytoplasmic Polyhedrosis Virus Protein Complex of a Polyhedrin and a VP3 Polypeptide--.

Claim Objection

[7] Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

According to the specification, "The restricted region of VP3 is either a region from the N-terminus to the 40th amino acid residue or the region from the 41st amino acid residue to the 79th amino acid residue" (p. 6, second paragraph). According to *Toro Co. v. White Consolidated Industries Inc.,* 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999), "Where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim". Since the specification appears to specifically define the "restricted region" as noted above and since this definition would appear to "control interpretation of the term as it is used in the claim", claim 2 does not further limit claim 1.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

[8] Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a protein complex comprising a polyhedral protein having an insect virus encapsulated therein and a target protein having a restricted region of a capsid protein VP3 of cytoplasmic polyhedrosis virus as an embedding signal for polyhedron. When one considers a *Bombyx mori* cytoplasmic polyhedrosis virus (BmCPV) VP3 polypeptide as being the "target protein having a restricted region of a capsid protein VP3 of cytoplasmic polyhedrosis virus as an embedding signal for polyhedron", the claims read on a product of nature, *i.e.,* a

naturally-occurring BmCPV polyhedra, and should be amended to indicate the hand of the inventor, e.g., by insertion of "purified" or "isolated". See MPEP § 2105.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[9] Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

According to MPEP 2173.05(b), "A claim may be rendered indefinite by reference to an object that is variable." Claim 2 is indefinite as referencing particular amino acid positions within a CPV "VP3" polypeptide without providing a reference amino acid sequence in the claim, *e.g.,* by reference to a sequence identifier. In this case, the existence of more than one CPV VP3 polypeptide was known in the art at the time of the invention. See, *e.g.,* Appendix A, showing an alignment of *B. mori* CPV strain H VP3 (query 2) and *B. mori* CPV strain 1 VP3 (query 1), wherein the amino acid sequences are not identical. As such, a skilled artisan would recognize that the particular amino acid sequence at a noted position is variable and is dependent upon the particular amino acid sequence of the VP3 polypeptide. It is suggested that applicant clarify the particular amino acid sequence that is referenced in the claim.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[10] Claims 1-4 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

According to MPEP 2163.II.A.1, in evaluating a claimed invention for adequate written description, the examiner should determine what the claim as a whole covers. "Claim construction is an essential part of the examination process. Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description. See, e.g., *In re Morris*, 127 F.3d 1048, 1053-54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997)."

The claims are drawn to a genus of protein complex comprising any polyhedral protein having an insect virus encapsulated therein and a target protein having a "restricted region" of a capsid protein VP3 of cytoplasmic polyhedrosis virus as an embedding signal for polyhedron.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the claimed or recited genus of protein complexes, i.e., a protein complex of a target protein fused to the C-terminus of full-length BmCPV strain H VP3 protein occluded within the BmCPV strain H polyhedrin. Other than this single species, the specification fails to disclose other representative species of the genus of claimed protein complexes. In this case, the genus of protein complexes encompasses widely variant species, including a protein complex of any target protein "having a restricted region of a capsid protein VP3" of any CPV as an embedding signal for polyhedron. The disclosure of the single representative species of protein complexes as noted above fails to reflect the variation among the members of the genus. In this case, the genus of protein complexes is required to have the structural feature of a "restricted region" which functions "as an embedding signal for

polyhedron". However, the specification characterizes only one such structure-function relationship, *i.e.,* the "restricted region" of BmCPV strain H VP3, which is defined in the specification as "either a region from the N-terminus to the 40th amino acid residue or the region from the 41st amino acid residue to the 79th amino acid residue" (p. 6, second paragraph).

Although it is acknowledged that the claims are unlimited with respect to CPV that is the source of the VP3 protein, it is noted that even among *Bombyx mori* CPV, Hagiwara et al. (*J. Gen. Virol.* 83:1477-1482, 2002; cited as reference AO in the IDS filed on 7/8/05) discloses that *B. mori* CPVs "can be divided into nine strains...distinguished by the shapes and/or the intracellular localization of the inclusion bodies" (p. 1477, column 2, top). Given that the specification discloses only a single representative species of the genus of VP3 polypeptides, *i.e.,* BmCPV strain H VP3, the corresponding BmCPV strain H polyhedrin, and the structure-function relationship between the "restricted region" of BmCPV strain H VP3 and its function of being an "embedding signal" for the BmCPV strain H polyhedrin, the species encompassed by the genus are widely variant and given the lack of description of a representative number of compounds sufficient to reflect that variation, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[11] Claim(s) 1-4 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein complex of a target protein fused to the C-terminus of full-length *Bombyx mori* CPV strain H VP3 protein occluded within the *Bombyx mori* CPV strain H polyhedrin, does not reasonably provide enablement for all protein complexes as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: According to MPEP 2164.04, "[b]efore any analysis of enablement can occur, it is necessary for the examiner to construe the claims...and

explicitly set forth the scope of the claim when writing an Office action." MPEP 2164.08 states, "[a]ll questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. Accordingly, the first analytical step requires that the examiner determine exactly what subject matter is encompassed by the claims...claims are to be given their broadest reasonable interpretation that is consistent with the specification."

The claims are so broad as to encompass any protein complex comprising a polyhedral protein having an insect virus encapsulated therein and a target protein having a restricted region of a capsid protein VP3 of cytoplasmic polyhedrosis virus as an embedding signal for polyhedron and a biosensor comprising said protein complex. The source of the polyhedrin is unlimited, while the source of the recited VP3 protein is limited to being a CPV VP3 polypeptide. Also, in view of the disclosure of the specification, it appears that applicant intends for "VP3" to encompass not only full-length proteins, but to also encompass fragments of CPV VP3 polypeptides. The broad scope of the claims is not commensurate with the enablement provided by the disclosure, particularly with regard to the CPV VP3 polypeptide and corresponding polyhedron, where the CPV VP3 polypeptide has a "restricted region...as an embedding signal for polyhedron". According to the specification, the "restricted region" is defined as "either a region from the N-terminus to the 40th amino acid residue or the region from the 41st amino acid residue to the 79th amino acid residue" (p. 6, second paragraph). In this case the disclosure is limited to a protein complex of a BmCPV strain

H polyhedral protein with an embedded target protein fused to the C-terminus of *Bombyx mori* CPV strain H VP3 protein.

The state of the prior art; The level of one of ordinary skill; The level of predictability in the art: Protein complexes of a target protein occluded by the polyhedra of *nuclear* polyhedrosis viruses are well-known in the prior art. However, application of this concept to other viruses, *e.g.,* CPVs, appears to require knowledge of those regions of the polyhedra that are non-essential for crystallization and interactions between the proteins of the polyhedron and proteins occluded thereby. In this case, Ikeda et al. (*supra*) and Ohta et al. (WO 02/36785; cited in the IDS filed on 7/8/05 as reference AF) disclose the sequence of the BmCPV H strain VP3 polypeptide. However, the prior art does not appear to characterize this interaction in any other CPVs as broadly encompassed by the claims. As noted in Ikeda et al. (*supra*), "little is known about the specific interactions between CPV polyhedron and the viral capsid protein," particularly the interaction between CPV polyhedron and VP3 (p. 994, column 1, middle). Thus, other than the interaction between BmCPV strain H polyhedrin and VP3, there is no way to predict interaction of any VP3 protein of any strain of *Bombyx mori* CPV with any other strain of *B. mori* CPV polyhedrin to achieve a protein complex as encompassed by the claims. Furthermore, it is noted that the post-filing reference of Mori et al. (*J. Biol. Chem.* 282:1728917296, 2007; "Mori"), in disclosing production of *B. mori* CPV polyhedra containing human FGF-2, teaches that "only degradation products of FGF-2 were found in polyhedra where FGF-2 was fused with VP3 at the N terminus" (p. 17292, column 1, first paragraph). Moreover, as evidenced by the instant specification, C-

terminal deletions of VP3 disrupt immobilization of a target protein into polyhedra (Figure 3).

The amount of direction provided by the inventor; The existence of working examples: The specification's only example of the claimed protein complex is a protein complex of a target protein fused to the C-terminus of BmCPV strain H VP3 embedded within the BmCPV strain H polyhedrin. Other than this working example, the specification fails to provide the necessary specific guidance for isolating other BmCPV VP3 polypeptides. Further, the specification fails to provide guidance for interchanging the VP3 protein from one strain of CPV with the polyhedrin of any other virus with an expectation of achieving a protein complex as encompassed by the claims.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the state of the art regarding interaction between viral polyhedrin and CPV VP3 proteins, and the high level of unpredictability as noted above, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily,

and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections – Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

[12] Claims 1-4 and 7-8 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 18 of co-pending Application No. 10/415,096, which corresponds to Ohta et al. (WO 02/36785; cited in the IDS filed on 7/8/05 as reference AF) as cited below. Claims 7-8 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 18 of co-pending Application No. 10/415,096 in view of Hosokawa et al. (Materials Research Society, Symposium C, Bio-Inspired Nanoscale Hybrid Systems, December 2002, Abstract C3.5) and Ito et al. (*Appl. Physics Lett.* 78:2566-2568, 2001).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-4 of the instant application are generic to all that is recited in claims 1-8 and 18 of the co-pending application, i.e., claims 1-4 of the instant application are anticipated by claims 1-8 and 18 of the co-pending application. Also, the biosensors of claims 7-8 herein are obvious variants of the protein complex of claims 1-8 and 18 of the co-pending application and the biosensor of claim 6 is obvious in view of the protein complex of claims 1-8 and 18 of the co-pending application in view of Hosokawa et al. and Ito et al. for reasons set forth below.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[13] Claim(s) 1-4 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ohta et al. (WO 02/36785; cited in the IDS filed on 7/8/05 as reference AF; "Ohta"). Since the Ohta reference is a non-English language document, reference to the corresponding US Patent Application Publication 2004/0059091 (cited in the IDS filed on 7/8/05 as reference AA) will be used as an English-language equivalent of the Ohta reference, particularly as the IDS filed on 7/8/05 indicates that US Patent Application Publication 2004/0059091 is a translation of the Ohta reference. According to MPEP 2112.III, "Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection."

The claims are drawn to a protein complex comprising a polyhedral protein having an insect virus encapsulated therein and a target protein having a restricted region of a capsid protein VP3 of cytoplasmic polyhedrosis virus as an embedding signal for polyhedron.

The reference of Ohta teaches a protein complex of *B. mori* CPV (BmCPV) strain H polyhedra with occluded BmCPV VP3 fused to GFP (p. 8, paragraph 110). Also, according to Ohta, "the protein complex...with the objective protein occluded with polyhedrin...where polyhedrin contributes to improvement of stability, or protection, or improvement of preservability of the objective protein, or combination thereof" (p. 2, paragraph 23). Ohta teaches the GFP of the *B. mori* H strain CPV VP3-GFP chimeric protein exhibited green fluorescence and thus would be considered a "fluorescent or light-emitting" protein by one of ordinary skill in the art.

According to Ohta, "It has been demonstrated that virions enter specifically into the polyhedra because of the specific relation between the viral occlusion body protein of virions and polyhedrin" (p. 1, paragraph 17), thus, although Ohta does not expressly teach the protein complex has an encapsulated virion(s), this would be a necessary feature of the protein complex of Ohta. Also, although Ohta does not teach the BmCPV strain H VP3 of the VP3-GFP chimeric protein has a "restricted region...as an embedding signal for polyhedron", or a has a "restricted region" as defined in claim 2, since the chimeric protein of Ohta has an intact N-terminus and is occluded by the BmCPV strain H polyhedra (*e.g.*, p. 8, paragraph 104), one of ordinary skill in the art

would recognize that the VP3 of the chimeric protein of Ohta necessarily has such a "restricted region".

This anticipates claims 1-4 as written.

[14] Claim(s) 1-4 and 6-8 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Mori et al. (JP 2003-155300, 2003; "Mori"). The cited teachings below are based on a raw machine English translation of obtained at www.ipdl.inpit.go.jp/homepg_e.ipdl on 12/16/07.

The claims are drawn to a protein complex comprising a polyhedral protein having an insect virus encapsulated therein and a target protein having a restricted region of a capsid protein VP3 of cytoplasmic polyhedrosis virus as an embedding signal for polyhedron and a biosensor.

The reference of Mori teaches a protein complex of BmCPV strain H polyhedra with occluded BmCPV VP3 fused to GFP (p. 6, paragraph 27), wherein the occluded protein is stabilized (p. 7, bottom to p. 8, top). Mori teaches a protein chip having a microcell with the protein complex affixed thereto (pp. 9-10). Mori teaches the arrangement of the protein complex on array can in a line (Figure 8 and p. 11) further teaches that a protein complex and a chemical can react (p. 11, bottom). Since the array comprising the VP3-GFP chimera of Mori was able to show GFP fluorescence, it is considered to be "packed in such a manner that it can be contacted with a substance in a test solution in a recess formed on a substrate" (claim 7) and ". Claim 8 "packed in

a container in such a manner that it can be contacted with a substance in a test solution".

According to Mori, "This virus has the description of producing the crystal...and is called a polyhedron to the cytoplasm of the infected cell. Embedding of much virions is carried out to this polyhedron" (p. 4, paragraph 23), thus, although Mori does not expressly teach the protein complex has an encapsulated virion(s), one of ordinary skill in the art would recognize this would be a necessary feature of the protein complex of Mori. Also, although Mori does not expressly teach the BmCPV strain H VP3 of the VP3-GFP chimeric protein has a "restricted region...as an embedding signal for polyhedron", or a has a "restricted region" as defined in claim 2, since the chimeric protein of Mori is occluded by the BmCPV strain H polyhedra (*e.g.,* p. 5, paragraph 24), one of ordinary skill in the art would recognize that the VP3 of the chimeric protein of Mori necessarily has such a "restricted region".

This anticipates claims 1-4 and 6-8 as written.

Claim Rejections - 35 USC § 103

[15] Claim(s) 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ohta (*supra*) in view of Hosokawa et al. (Materials Research Society, Symposium C, Bio-Inspired Nanoscale Hybrid Systems, December 2002, Abstract C3.5; available at www.mrs.org/s_mrs/bin.asp?CID=2109&DID=91203&DOC=FILE.PDF; "Hosokawa") and Ito et al. (*Appl. Physics Lett.* 78:2566-2568, 2001; "Ito").

Claim 6 is drawn to a biosensor "characterized in that a protein complex according to claim 1 is arranged in dots or lines on a substrate and immobilized thereon".

The reference of Ohta teaches a protein complex as noted above. Ohta does not teach a biosensor as set forth in claim 6.

The reference of Hosokawa teaches, "The proteomics technique has received significant attention as an important technique for disease diagnosis and for monitoring drug efficacy and safety. To realize the high-throughput analysis of proteins expression, preparation of protein microarrays is strongly requested, however, it is very difficult in comparison with DNA microarrays because of complex structures of proteins. Recently, we have been interested in applying protein crystal of polyhedra, which are μm-size proteinaceous occlusion bodies produced by insect viruses, for immobilization of functional proteins. On the other hand, a laser trapping technique based on the photon pressure has received much attention as a technique to manipulate biocells and microparticles. Recently, furthermore, we have already succeeded photothermal fixation of polymer microparticles onto a polymer substrate by local heating due to UV laser irradiation. It is considered that the polyhedra crystals are very useful to fabricate protein microarrays and we demonstrated here that the polyhedra crystals of a few μm could be fixed one by one on a slide glass by laser manipulation technique. Aqueous solution containing the dispersed polyhedra crystals was set on the microscope stage and each crystal was trapped by a focused 1064 nm beam of a Nd^{3+} : YAG laser. On the trapped polyhedra, femtosecond laser was irradiated to fix it on a polymer substrate.

Damages of the polyhedra crystals will be decreased by adjusting femtosecond laser and noncontact pattering of the polyhedra crystal is realized with the precision less than 1 μm".

Ito discloses a method for fixing nanoparticles onto a glass substrate using a 1064 nm Nd^{3+} : YAG laser (pp. 2566-2567), wherein the nanoparticles comprise a fluorescent dye (2566, column 2), and the nanoparticles are placed onto the glass substrate in a dot or a line (p. 2567, Figures 1-3). Ito further teaches "The present method will be extended" to "hopefully" fix "biological molecules" (p. 2568, column 1).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Ohta, Hosokawa, and Ito for a protein microarray of the protein complex of Ohta affixed to a glass substrate in dots or lines. One would have been motivated to do this because Hosokawa expressly teach doing this using a polyhedra crystal and the protein complex of Ohta, having an embedded GFP, would have provided a means for monitoring whether or not the protein crystal was fixed to the glass substrate, and Ito, which teaches fixing the fluorescent nanoparticles in dots or lines as noted above. One would have a reasonable expectation of success for a protein microarray of the protein complex of Ohta affixed to a glass substrate according to the methods of Hosokawa and Ito because of the results of Ohta, Hosokawa, and Ito. Therefore, claim 6, drawn to a biosensor as described above would have been obvious to one of ordinary skill in the art at the time of the invention.

[16] Claim(s) 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohta (*supra*). Claim 7 is drawn to a biosensor "characterized in that a protein complex according to claim 1 is packed in such a manner that it can be contacted with a substance in a test solution in a recess formed on a substrate". Claim 8 is drawn to a biosensor "characterized in that a protein complex according to claim 1 is packed in a container in such a manner that it can be contacted with a substance in a test solution".

The reference of Ohta teaches a protein complex as noted above. Ohta does not expressly teach a biosensor as set forth in claims 7-8.

Regarding claim 7, the phrase "packed in such a manner that it can be contacted with a substance in a test solution in a recess formed on a substrate", the term "packed" has been interpreted as meaning "packaged" and "a recess formed on a substrate" has been interpreted as encompassing a 96-well plastic microplate, which were well-known to one of ordinary skill in the art at the time of the invention. Although Ohta does not expressly teach the protein complex in solution in a 96-well microplate, one of ordinary skill in the art would recognize that that protein complex of Ohta would have been placed in wells of a 96-well microplate for simultaneous analysis of multiple samples, *e.g.*, during the pH analysis as set forth at p. 8, paragraph 107.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to place a solution of the protein complex of Ohta in a well of a microplate. One would have been motivated to do this in order to simultaneously prepare multiple samples for analysis. One would have had a reasonable expectation of success to place a solution of the protein complex of Ohta in a well of a 96-well

microplate because of the results of Ohta. Therefore, claim 7, drawn to a biosensor as described above would have been obvious to one of ordinary skill in the art at the time of the invention.

Regarding claim 8, the phrase "packed in a container in such a manner..." has been broadly, but reasonably interpreted as meaning the protein complex is present in a solution in a test tube, *e.g.,* a microfuge tube, which were well-known to one of ordinary skill in the art at the time of the invention. Although Ohta does not expressly teach the protein complex was in solution in a container, one of ordinary skill in the art would have recognized that that protein complex of Ohta would have been stored in a microfuge tube, for storage and preparation of the sample for analysis, *e.g.,* pH analysis as set forth at p. 8, paragraph 107.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to place a solution of the protein complex of Ohta in a microfuge tube. One would have been motivated to do this in order to store the protein complex and prepare the protein complex for analysis. One would have had a reasonable expectation of success to place a solution of the protein complex of Ohta in a microfuge tube because of the results of Ohta. Therefore, claim 8, drawn to a biosensor as described above would have been obvious to one of ordinary skill in the art at the time of the invention.

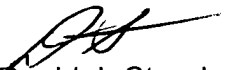
Conclusion

[17] Status of the claims:

- Claims 1-9 are pending.
- Claims 5 and 9 are withdrawn from consideration.
- Claims 1-4 and 6-8 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656

APPENDIX A

Query sequence 1

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Query sequence 2

>Seq2
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Full-length alignment between two sequences

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s-w opt: 6782 Z-score: 8324.2 bits: 1551.9 E(): 0
Smith-Waterman score: 6782; 98.677% identity (98.770% ungapped) in 1058 aa overlap (1-1058:7-1063)

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